

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/21769

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C12Q 1/68; C07H 21/02, 21/04  
US CL :435/6; 536/23.1, 23.5

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6; 536/23.1, 23.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

USPT, DWPI, MEDLINE, CAPLUS, LIFESCI, SCISEARCH, BIOSIS, EMBASE  
search terms: interleukin 10, IL10, promoter, allele, polymorphism, mutation, SNP, genotype, -3575, -2849, -2763

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	AHERN, H. Biochemical, reagent kits offer scientists good return on investment. <i>The Scientist</i> . 24 July 1995, Vol. 9, No. 15, p. 20, especially p. 3/5-4/5.	9
X	ESKDALE et al. Mapping of the human IL10 gene and further characterization of the 5' flanking sequence. <i>Immunogenetics</i> . August 1997, Vol. 46, No. 2, pages 120-128, especially Fig. 1, Fig. 4.	1, 10
Y		-----
---		9
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A		2-8, 11
X	MOK et al. Interleukin-10 promoter polymorphisms in southern Chinese patients with systematic lupus erythematosus. <i>Arthritis &amp; Rheumatism</i> . June 1998, Vol. 41, No. 6, pages 1090-1095, especially Table 3.	3, 7-8
Y		-----
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A		1-2, 4-6, 10-11

Further documents are listed in the continuation of Box C.  See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"		document defining the general state of the art which is not considered to be of particular relevance
"E"	"X"	earlier document published on or after the international filing date
"L"	"Y"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O"		document referring to an oral disclosure, use, exhibition or other means
"P"	"&"	document published prior to the international filing date but later than the priority date claimed

Date of the actual completion of the international search

26 SEPTEMBER 2000

Date of mailing of the international search report

24 OCT 2000

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Faxsimile No. (703) 305-3230

Authorized officer

DIANA B. JOHANNSEN

Telephone No. (703) 308-0196

## INTERNATIONAL SEARCH REPORT

International application No. PCT/US00/21769
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## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----	<b>ROOD et al.</b> <i>Neuropsychiatric systematic lupus erythematosus is associated with imbalance in interleukin 10 promoter haplotypes.</i> <i>Ann. Rheum. Dis.</i> February 1999, Vo. 58, No. 2, pages 85-89, <i>especially p. 87-88.</i>	3, 7-8 -----
Y ----		9 -----
A		1-2, 4-6, 10-11
A	<b>COAKLEY et al.</b> <i>Interleukin-10 promoter polymorphisms in rheumatoid arthritis and Felty's syndrome.</i> <i>Brit. J. Rheum.</i> September 1998, Vol. 37, No. 9, pages 988-991.	1-11
A	<b>MYTILINEOS et al.</b> <i>A PCR-SSP method for the detection of polymorphisms in the promoter regions of IL10, TNFA, and TGFB genes.</i> <i>Human Immunol.</i> April 1999, Vol. 60, No. SUPPL 1, page S104.	1-11
A	<b>KEIJRSERS et al.</b> <i>IL10 polymorphisms in relation to production and rheumatoid arthritis.</i> <i>Arthritis &amp; Rheumatism.</i> September 1997, Vol. 40, No. 9 SUPPL, page S179.	1-11
A	<b>TOUNTAS et al.</b> <i>Ethnic association of 3 polymorphisms in the IL-10 promoter and inflammatory bowel disease (IBD).</i> <i>Gastroenterology.</i> April 1999, Vol. 116, No. 4, Part 2, page G3617.	1-11



## PATENT COOPERATION TREATY

PCT

**NOTIFICATION OF ELECTION**  
 (PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 10 July 2001 (10.07.01)
International application No. PCT/US00/21769
International filing date (day/month/year) 09 August 2000 (09.08.00)
<b>Applicant</b>  KIMBERLY, Robert, P. et al

**Applicant's or agent's file reference**  
UAB-16852/22

**Priority date (day/month/year)**  
09 August 1999 (09.08.99)

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

05 March 2001 (05.03.01)

in a notice effecting later election filed with the International Bureau on:

\_\_\_\_\_

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  H. Zhou
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: ELLEN S. COGEN  
 GIFFORD, KRASS, GROH, SPRINKLE, ANDERSON  
 & CITKOWSKI, P.C.  
 280 N. OLD WOODWARD AVE., STE 400  
 BIRMINGHAM, MI 48009  
 US

**PCT**

## NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Date of Mailing  
(day/month/year)

**24 OCT 2000**

Applicant's or agent's file reference  UAB-16852/22	FOR FURTHER ACTION    See paragraphs 1 and 4 below
International application No.  PCT/US00/21769	International filing date (day/month/year)  09 AUGUST 2000
Applicant  <b>UAB RESEARCH FOUNDATION</b>	<i>Response out 11-24-00 due 12-24-00</i>

1.  The applicant is hereby notified that the international search report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland  
 Facsimile No.: (41-22) 740.14.35

**For more detailed instructions**, see the notes on the accompanying sheet.

2.  The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

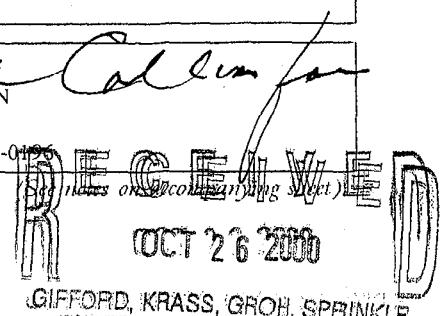
Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US  
 Commissioner of Patents and Trademarks  
 Box PCT  
 Washington, D.C. 20231  
 Facsimile No. (703) 305-3230

Authorized officer  
 DIANA B. JOHANNSEN

Telephone No. (703) 308-0156

Form PCT/ISA/220 (July 1998)★



GIFFORD, KRASS, GROH, SPRINKLE,  
 ANDERSON & CITKOWSKI, P.C.

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: ELLEN S. COGEN  
 GIFFORD, KRASS, GROH, SPRINKLE, ANDERSON  
 & CITKOWSKI, P.C.  
 280 N. OLD WOODWARD AVE., STE 400  
 BIRMINGHAM, MI 48009  
 US

**PCT**

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Date of Mailing  
(day/month/year)

**24 OCT 2000**

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International application No.  PCT/US00/21769	International filing date (day/month/year) 09 AUGUST 2000
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 34, chemin des Colombettes  
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- no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

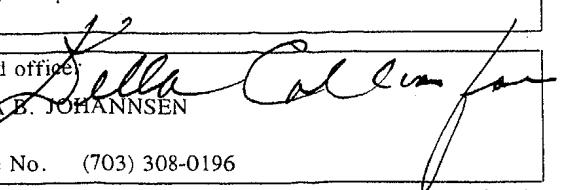
4. **Further action(s):** The applicant is reminded of the following:

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Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US  
 Commissioner of Patents and Trademarks  
 Box PCT  
 Washington, D.C. 20231  
 Facsimile No. (703) 305-3230

Authorized office:  
  
 DIANA B. JOHANNSEN  
 Telephone No. (703) 308-0196

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference UAB-16852/22	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US00/21769	International filing date (day/month/year) 09 AUGUST 2000	(Earliest) Priority Date (day/month/year) 09 AUGUST 1999	
Applicant <b>UAB RESEARCH FOUNDATION</b>			

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

contained in the international application in written form.

filed together with the international application in computer readable form.

furnished subsequently to this Authority in written form.

furnished subsequently to this Authority in computer readable form.

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of invention is lacking (See Box II).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. 3

as suggested by the applicant.

because the applicant failed to suggest a figure.

because this figure better characterizes the invention.

None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/21769

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

NEW ABSTRACT

*A process and a package for identifying single nucleotide polymorphisms in interleukin-10 (IL-10) are useful in identifying individual susceptibility to a disease. IL-10 is active in the immune response and autoimmune diseases. The susceptibility and severability of autoimmune disease is determined by genotyping or phenotyping an individual IL-10 promoter region. Figure 3 is a graph showing association of -3575A/-2763A SNP haplotype with production of IL-10 by donors, segregated by distal SNP haplotypes.*

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PCT/US00/21769

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/68; C07H 21/02, 21/04

US CL : 435/6; 536/23.1, 23.5

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6; 536/23.1, 23.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

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search terms: interleukin 10, IL10, promoter, allele, polymorphism, mutation, SNP, genotype, -3575, -2849, -2763

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	AHERN, H. Biochemical, reagent kits offer scientists good return on investment. <i>The Scientist</i> . 24 July 1995, Vol. 9, No. 15, p. 20, especially p. 3/5-4/5.	9
X	ESKDALE et al. Mapping of the human IL10 gene and further characterization of the 5' flanking sequence. <i>Immunogenetics</i> . August 1997, Vol. 46, No. 2, pages 120-128, especially Fig. 1, Fig. 4.	1, 10
Y		9
A		2-8, 11
X	MOK et al. Interleukin-10 promoter polymorphisms in southern Chinese patients with systematic lupus erythematosus. <i>Arthritis &amp; Rheumatism</i> . June 1998, Vol. 41, No. 6, pages 1090-1095, especially Table 3.	3, 7-8
Y		9
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Further documents are listed in the continuation of Box C.  See patent family annex.

Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
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## INTERNATIONAL SEARCH REPORT

International application No.  
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## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	<b>KEIJERSERS et al.</b> <i>IL10 polymorphisms in relation to production and rheumatoid arthritis.</i> <i>Arthritis &amp; Rheumatism.</i> September 1997, Vol. 40, No. 9 SUPPL, page S179.	1-11
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